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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/802,457	03/09/2001	Nonda Katopodis	NK3	7046

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EXAMINER	
CANELLA, KAREN A	

ART UNIT	PAPER NUMBER
1643	

DATE MAILED: 09/14/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/802,457	KATOPODIS, NONDA	
	Examiner	Art Unit	
	Karen A. Canella	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-18 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-18 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

C.D.O.

DETAILED ACTION

1. Claims 1, 17 and 18 have been amended. Claims 19 and 20 have been canceled. Claims 1-18 are pending and under consideration.

2. After review and reconsideration, the finality of the Office action mailed Oct 22, 2002, is withdrawn.

3. Text of Title 35, U.S. Code not found in this action can be found in a previous action.

4. Claim 8 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. the recitation of "sample" and "amount" in claim 8 lacks antecedent basis within claim 1. It is unclear what is being referred to in the context of the "sample". Further, it is unclear if the "predetermined amount" is the volume removed or the volume remaining.

5. Claims 1-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Katopodis (WO 92/08976) in view of Chondros et al (Anticancer Research, 1991, Vol. 11, pp. 2103-2106) and Stoscheck (Quantitation of Protein, In: Guide to Protein Purification, Deutscher, Ed., 1990, pp. 50-68) as evidenced by Jones et al (U.S. 5,236,927).

Claim 1 is drawn to a method of extracting lipid associated sialoprotein from the body fluids of human subjects having or suspected of having cancer, wherein said body fluids are selected from the group consisting of CSF, urine, saliva, sputum, peritoneal fluid, pleural fluid and bronchial washings; said method comprising determining the amount of lipid associated sialoprotein in a sample of said fluid comprising the following steps: (a) adding to the sample a mixture of chlorinated lower alkyl hydrocarbon and lower alkyl alcohol; (b) mixing the resulting admixture for a suitable period of time to dissolve lipid-bound sialic acid in the sample into the chlorinated hydrocarbon/ alcohol mixture; (c) centrifuging the mixture at about 6000 rpm to form a substantially clear upper phase; (d) separately recovering , a predetermined volume of cleared upper phase; (e) adding to the predetermined volume of the upper phase so obtained, an amount of a mixture of an aqueous protein-precipitating agent without any absorbing material,

the amount of said mixture being effective to cause precipitation of the lipid associated sialoprotein; (f) vortexing the resulting admixture; (g) centrifuging and recovering the resulting precipitate; (h) washing the precipitate in a saline solution; (i) centrifuging the resulting mixture; (j) dissolving the precipitate in water; (k) adding a hydrolyzing agent to the resulting solutions; (l) heating the resulting admixture; (m) determining the amount of lipid associated sialoprotein present in the solution and thereby the amount present in the fluid sample. Claim 2 embodies the method of claim 1 wherein in step (a) the volume of the added mixture is about 750 uL. Claim 3 embodies the method of claim 1, wherein the lower alky alcohol is methanol, ethanol. propanol, n-butanol, isopropanol, isobutanol, or isoamyl alcohol. Claim 4 embodi4es the method of claim 1 wherein the lower alkyl hydrocarbon is chloroform, methylene chloride or ethylene chloride. Claim 5 embodies the method of claim 1hwerein the mixing in step (b) takes place for at least 15 seconds. Claim 6 embodies the method of claim 1 wherein in step (c) the mixture is centrifuged at about 6000 rpm for at least 5 minutes. Claim 7 embodies the method of claim 1 wherein in step (d) the upper phase is removed from the lower phase. Claim 8 embodies the method of claim1 wherein in step (d) the predetermined amount of the upper phase is about the same as the volume of the sample. Claim 9 embodies the method of claim 1 wherein in step (e) the protein precipitating agent is phosphotungstic acid, trichloroacetic acid, ammonium sulfate of a mixture thereof. Claim 10 embodies the method of claim 1 wherein in step (e) the concentration of the protein precipitating agent is between 0.1 and 0.6 mg/mL. Claim 11 embodies the method of claim 1 wherein in step (f) the mixing takes place for at least 5 seconds. Claim 12 embodies the method of claim 1 wherein in step (h) the precipitate is washed with 500 uL of saline to remove trace contaminants. Claim 13 embodies the method of claim 1 wherein in step (k) the hydrolysis reagent is resorcinol. Claim 14 embodies the method of claim 1 wherein in step (l) the admixture is heated to 115-120 degrees C for 15 minutes. Claim 15 embodies the method of claim 1 wherein in step (m), the amount of lipid associated sialoprotein is determined by adding to the suspended precipitate a volume of resorcinol reagent, mixing, boiling for 15 min, adding a mixture of butyl acetate and n-butanol (85:15 v/v) in a volume about twice said volume of resorcinol, mixing, centrifuging for about 5 min at greater than 2500 rpm, separating the organic layer, reading at 580 nm the extracted blue color present in the organic layer, determining the amount of lipid associated sialoprotein by comparing the reading obtained at 580 nm to that

obtained for a standard having a known amount of lipid associated sialoprotein and applying the formula (A X B)/C, wherein A is the concentration of lipid associated sialoprotein in the standard, B is the optical density of the sample and C is the optical density of the standard. Claim 16 embodies the method of claim 15 wherein the volume of resorcinol is about 0.5 ml.

Claim 17 is drawn to a method of diagnosing cancer in a human subject which comprises determining the amount of lipid associated sialoprotein in a sample of said subjects CSF, urine, saliva, sputum, peritoneal fluid, pleural fluid or bronchial washings according to the method of claim 1, and comparing the amount so determined with amounts previously obtained for subjects known to have cancer.

Claim 19 is drawn to a method of diagnosing cancer in a human subject comprising determining at regular time intervals the amount of lipid-associated sialoprotein in a sample of said subjects CSF, urine, saliva, sputum, peritoneal fluid, pleural fluid or bronchial washings according to the method of claim 1, and comparing the amounts so determined with amounts previously obtained for said subject.

Katopodis teaches a method of extracting lipid bound sialic acid from human blood plasma or serum and determining the amount of lipid bound sialic acid in a sample of human blood plasma or serum which comprises the following steps: a) diluting a predetermined volume of 25 microliters or less of a blood plasma or serum sample with distilled water to a volume about two times that of the predetermined volume of the sample; b) mixing the diluted sample for a suitable period of time to obtain a substantially homogeneous sample; c) adding to the sample a mixture of a chlorinated lower alkyl hydrocarbon and a lower alkyl alcohol, the volume of the mixture added being about forth times the predetermined volume of the blood plasma or serum sample, and the volume ratio of chlorinated hydrocarbon to alcohol in the mixture being about 2:1; d) mixing the resulting admixture for a suitable period of time to dissolve lipid-bound sialic acid in the sample in the chlorinated hydrocarbon/alcohol mixture; e) diluting the admixture with a buffer solution at room temperature, the volume of buffer solution being about eight times the predetermined volume of the blood plasma or serum sample; f) mixing the diluted admixture without vortexing for a suitable period of time to obtain a substantially homogeneous admixture and centrifuging the mixture to form a substantially clear upper phase; g) separately recovering from the clear upper phase so formed a predetermined volume of the upper phase; h)

adding to the predetermined volume of the upper phase an amount of a mixture of a protein-precipitating agent and water without any adsorbing material, the amount of mixture being effective to cause precipitation of the lipid bound sialic acid; i) mixing the resulting admixture; j) separately recovering the resulting precipitate; k) suspending the precipitate in a hydrolysis agent; l) determining the amount of lipid bound sialic acid present in the suspended precipitate and thereby the amount present in the blood plasma or serum sample (claim 1). Katopodis teaches the volume of the added mixture is about 1 ml. Katopodis teaches that the term "about" refers to a range of values up to 200% of a specified value (page 8, lines 30-33), therefore 1 ml meets the specific limitation of claim 2, requiring 0.75 mL. Katopodis teaches the mixing of the sample in part (b) to obtain a suitable homogenous sample, for at least 30 seconds (page 9, lines 32-34), which fulfills the specific embodiment of claim 5. Katopodis teaches centrifuging the mixture of part (c) at above 3500 rpm, which meets the specific embodiment of about 6000 rpm, because Katopodis teaches that the term about encompasses values up to 200% the stated value. Katopodis teaches lower alkyl alcohol is methanol, ethanol, propanol, n-butanol, isopropanol, isobutanol or isoamyl alcohol (claim 3) and lower chlorinated hydrocarbons are chloroform, methylene chloride or ethylene chloride (claim 4), thus fulfilling the specific embodiments of claims 3 and 4. Katopodis teaches the removal of the upper phase from the lower phase (claim 8) thus fulfilling the specific embodiments of claim 7. Katopodis teaches the addition of 0.2 ml of buffer to a 25 uL sample (page 9, lines 29-31) and removal of a predetermined volume of 0.2 ml after formation of the cleared upper phase (page 10, lines 9-10), thus fulfilling the specific embodiment of claim 8. Katopodis teaches the protein precipitating agents of phosphotungstic acid, trichloroacetic acid and ammonium sulfate (claim 10). Katopodis teaches the concentration of protein precipitating agent between 0.3 and 0.6 mg/mL (claim 11). Katopodis teaches resorcinol as a hydrolysis agent (claim 14) and heating of the admixture of step (l) to "about" 115-120 degrees C for 15 minutes (page 10, lines 33-35) which fulfills the specific embodiment of claim 14 as the term "about" encompasses 50% to 200% of the recited limitation. Katopodis teaches boiling for 15 minutes after the addition of resorcinol (page 10, lines 32-33), the addition of butyl acetate and n-butanol (85:15 v/v) (page 11, lines 4-5) in twice said volume of resorcinol reagent (page 11,lines 1-2), centrifuging for at least 5 minutes at above 2500 rpm, separating the organic layer, reading at 580 nm the extracted blue color present in the organic layer,

determining the amount of lipid associated sialoprotein by comparing the reading obtained at 580 nm to that obtained for a standard having a known amount of lipid associated sialoprotein and applying the formula (A X B)/C (page 11, lines 6-18). Katopodis teaches a method of diagnosing cancer in a human subject which comprises determining the amount of lipid bound sialic acid in a sample of the subject's blood plasma or serum according to the method of claim 1 and comparing the amount so determined with values obtained for subjects known to have cancer (claim 21) and a method of diagnosing cancer in a human subject which comprises determining at regular time intervals the amount of lipid bound sialic acid in a sample of the subject's blood plasma or serum according to the method of claim 1 and comparing the amounts so determined with amounts previously obtained for the subject (claim 22), thus fulfilling the specific embodiments of claims 17 and 18. Katopodis teaches the extraction of lipid associated sialoprotein from human plasma or serum., and the vortexing of the sample in part (f) at least 3 second, rather than 5 seconds as stated in claim 11. Katopodis does not specifically teach washing of the precipitated protein in a saline solution (step h). Katopodis does not teach the extraction of lipid associated sialoprotein from CSF, urine, saliva, sputum, peritoneal fluid, pleural fluid and bronchial washings.

Chondros et al teach that the determination of total, lipid and bound sialic acid in body fluids other than serum has equally high sensitivity and specificity as the determination of total, lipid and bound sialic acid in serum(page 2105, column 1, lines 1-5 under the heading "Discussion"). Chondros et al teach the measurement of total, lipid and bound sialic acid in peritoneal fluid, pleural fluid and bronchial washings (Table I).

Stoscheck teaches that in many applications the solution containing the protein contains a mixture of components which can interfere with the measurement of protein, and that the interfering agent can be removed to facilitate the assay (page 57, last paragraph under "Colorimetric Assays"). Jones et al teaches a phosphate buffered saline wash after protein precipitation by trichloroacetic acid (column 21, lines 49-51).

It would have been prima facie obvious at the time the invention was made to substitute body fluids such as peritoneal fluid, pleural fluid and bronchial washings for the blood serum in the methods taught by Katopodis. One of skill in the art would have been motivated to do so by the teachings of Chondros et al on the presence of protein bound sialic acids in said fluids and

the teachings that fluids other than serum has equally high sensitivity and specificity as the determination of total, lipid and bound sialic acid.

Regarding the specific limitation of claim 1, sections (h) and claim 12 regarding the washing of the precipitate with saline, it is noted that optimization of the experimental protocol is within the purview of one of skill in the art, as exemplified by the teachings of Stoscheck regarding the removal of interfering components from protein before protein assays, and the example of Jones et al wherein proteins precipitated by trichloroacetic acid are washed by phosphate buffered saline.

6. Claims 1-7, 9-13, 15-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Katopodis et al (U.S. 5,296,346) in view of Chondros et al (Anticancer Research, 1991, Vol. 11, pp. 2103-2106) and Stoscheck (Quantitation of Protein, In: Guide to Protein Purification, Deutscher, Ed., 1990, pp. 50-68) as evidenced by Jones et al (U.S. 5,236,927).

The specific embodiments of the claims are recited above. Katopodis teaches a method of extracting lipid bound sialic acid from human blood plasma or serum and determining the amount of lipid bound sialic acid in a sample of human blood plasma or serum which comprises the following steps: a) diluting a predetermined volume of 25 microliters or less of a blood plasma or serum sample with distilled water to a volume about two times that of the predetermined volume of the sample; b) mixing the diluted sample for a suitable period of time to obtain a substantially homogeneous sample; c) adding to the sample a mixture of a chlorinated lower alkyl hydrocarbon and a lower alkyl alcohol, the volume of the mixture added being about forth times the predetermined volume of the blood plasma or serum sample, and the volume ratio of chlorinated hydrocarbon to alcohol in the mixture being about 2:1; d) mixing the resulting admixture for a suitable period of time to dissolve lipid-bound sialic acid in the sample in the chlorinated hydrocarbon/alcohol mixture; e) diluting the admixture with a buffer solution at room temperature, the volume of buffer solution being about eight times the predetermined volume of the blood plasma or serum sample; f) mixing the diluted admixture without vortexing for a suitable period of time to obtain a substantially homogeneous admixture and centrifuging the mixture to form a substantially clear upper phase; g) separately recovering from the clear upper phase so formed a predetermined volume of the upper phase; h) adding to the

predetermined volume of the upper phase an amount of a mixture of a protein-precipitating agent and water without any adsorbing material, the amount of mixture being effective to cause precipitation of the lipid bound sialic acid; i) mixing the resulting admixture; j) separately recovering the resulting precipitate; k) suspending the precipitate in a hydrolysis agent; l) determining the amount of lipid bound sialic acid present in the suspended precipitate and thereby the amount present in the blood plasma or serum sample (claim 1).

Katopodis teaches a method of extracting lipid bound sialic acid from human blood plasma or serum and determining the amount of lipid bound sialic acid in a sample of human blood plasma or serum which comprises the following steps: a) diluting a predetermined volume of 25 microliters or less of a blood plasma or serum sample with distilled water to a volume about two times that of the predetermined volume of the sample; b) mixing the diluted sample for a suitable period of time to obtain a substantially homogeneous sample; c) adding to the sample a mixture of a chlorinated lower alkyl hydrocarbon and a lower alkyl alcohol, the volume of the mixture added being about forth times the predetermined volume of the blood plasma or serum sample, and the volume ratio of chlorinated hydrocarbon to alcohol in the mixture being about 2:1; d) mixing the resulting admixture for a suitable period of time to dissolve lipid-bound sialic acid in the sample in the chlorinated hydrocarbon/alcohol mixture; e) diluting the admixture with a buffer solution at room temperature, the volume of buffer solution being about eight times the predetermined volume of the blood plasma or serum sample; f) mixing the diluted admixture without vortexing for a suitable period of time to obtain a substantially homogeneous admixture and centrifuging the mixture to form a substantially clear upper phase; g) separately recovering from the clear upper phase so formed a predetermined volume of the upper phase; h) adding to the predetermined volume of the upper phase an amount of a mixture of a protein-precipitating agent and water without any adsorbing material, the amount of mixture being effective to cause precipitation of the lipid bound sialic acid; i) mixing the resulting admixture; j) separately recovering the resulting precipitate; k) suspending the precipitate in a hydrolysis agent; l) determining the amount of lipid bound sialic acid present in the suspended precipitate and thereby the amount present in the blood plasma or serum sample (claim 1).

Katopodis teaches the volume of the added mixture is about 1 ml (claim 3) which fulfills the specific embodiments of the instant claim 2, requiring about 0.75 mL. Katopodis teaches the

mixing of the sample in part (b) to obtain a suitable homogenous sample, for at least 30 seconds (column 6, lines 56-58), which fulfills the specific embodiment of claim 5. Katopodis teaches lower alkyl alcohol is methanol, ethanol, propanol, n-butanol, isopropanol, isobutanol or isoamyl alcohol (claim 4) and lower chlorinated hydrocarbons are chloroform, methylene chloride or ethylene chloride (column 6, lines 31-33), thus fulfilling the specific embodiments of claims 3 and 4. Katopodis teaches the mixing of the sample and the chlorinated lower hydrocarbon solvent and the lower alcohol for at least 10 seconds (claim 7) which fulfills the specific embodiments of the instant claim 11. Katopodis teaches the removal of the upper phase from the lower phase (claim 10) thus fulfilling the specific embodiments of claim 7. Katopodis teaches the protein precipitating agents of phosphotungstic acid, trichloroacetic acid and ammonium sulfate (claim 12). Katopodis teaches the concentration of protein precipitating agent between 0.3 and 0.6 mg/mL (claim 13). Katopodis teaches resorcinol as a hydrolysis agent (claim 16). Katopodis teaches boiling for 15 minutes after the addition of resorcinol (page 10, lines 32-33), the addition of butyl acetate and n-butanol (85:15 v/v) in twice said volume of resorcinol reagent, centrifuging for at least 5 minutes at above 2500 rpm, separating the organic layer, reading at 580 nm the extracted blue color present in the organic layer, determining the amount of lipid associated sialoprotein by comparing the reading obtained at 580 nm to that obtained for a standard having a known amount of lipid associated sialoprotein and applying the formula (A X B)/C (claim 15). Katopodis teaches a method of diagnosing cancer in a human subject which comprises determining the amount of lipid bound sialic acid in a sample of the subject's blood plasma or serum according to the method of claim 1 and comparing the amount so determined with values obtained for subjects known to have cancer (claim 21) and a method of diagnosing cancer in a human subject which comprises determining at regular time intervals the amount of lipid bound sialic acid in a sample of the subject's blood plasma or serum according to the method of claim 1 and comparing the amounts so determined with amounts previously obtained for the subject (claim 22), thus fulfilling the specific embodiments of claims 17 and 18.

Katopodis teaches the extraction of lipid associated sialoprotein from human plasma or serum. and centrifugation of a mixture of sample, lower chlorinated hydrocarbons and lower alcohols at a speed greater than 3500 rpm. Katopodis does not specifically teach washing of the precipitated protein in a saline solution (step h) or the specific centrifugation speed of 6000 rpm.

Katopodis does not teach the extraction of lipid associated sialoprotein from CSF, urine, saliva, sputum, peritoneal fluid, pleural fluid and bronchial washings.

Chondros et al teach that the determination of total, lipid and bound sialic acid in body fluids other than serum has equally high sensitivity and specificity as the determination of total, lipid and bound sialic acid in serum(page 2105, column 1, lines 1-5 under the heading "Discussion"). Chondros et al teach the measurement of total, lipid and bound sialic acid in peritoneal fluid, pleural fluid and bronchial washings (Table I).

Stoscheck teaches that in many applications the solution containing the protein contains a mixture of components which can interfere with the measurement of protein, and that the interfering agent can be removed to facilitate the assay (page 57, last paragraph under "Colorimetric Assays"). Jones et al teaches a phosphate buffered saline wash after protein precipitation by trichloroacetic acid (column 21, lines 49-51).

It would have been prima facie obvious at the time the invention was made to substitute body fluids such as peritoneal fluid, pleural fluid and bronchial washings for the blood serum in the methods taught by Katopodis. One of skill in the art would have been motivated to do so by the teachings of Chondros et al on the presence of protein bound sialic acids in said fluids and the teachings that fluids other than serum has equally high sensitivity and specificity as the determination of total, lipid and bound sialic acid. Regarding the specific limitation of claim 1, section (h) and claim 12 regarding the washing of the precipitate with saline, it is noted that optimization of the experimental protocol is within the purview of one of skill in the art, as exemplified by the teachings of Stoscheck regarding the removal of interfering components from protein before protein assays, and the example of Jones et al wherein proteins precipitated by trichloroacetic acid are washed by phosphate buffered saline.

Regarding the specific limitation of claim 1, sections (c) and claim 6 regarding the speed of centrifugation, it is noted that optimization of the experimental protocol is within the purview of one of skill in the art. Thus, it would have been prima facie obvious at the time the clamed invention was made that a centrifugation speed of 6000 rpm was obvious over the limitation of claim 9, in '346 specifying that centrifugation was carried out at about 3500 rpm for the extraction of lipid associated sialoprotein from bodily fluids.

7. Claims 1-7, 9-13, 15-18 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims of U.S. Patent No. 5,296,346 in view of Chondros et al (Anticancer Research, 1991, Vol. 11, pp. 2103-2106) and Stoscheck (Quantitation of Protein, In: Guide to Protein Purification, Deutscher, Ed., 1990, pp. 50-68) as evidenced by Jones et al (U.S. 5,236,927). .

An obviousness-type double-patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g. In reBerg, 140 F.3d, 1428, 46 USPQ2d 1226 (Fed. Cir. 1998): In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993): In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). In the instant case, the pending claims are obvious over the claims of the '346 patent.

Katopodis claims the extraction of lipid associated sialoprotein from human plasma or serum. and centrifugation of a mixture of sample, lower chlorinated hydrocarbons and lower alcohols at a speed greater than 3500 rpm. Katopodis does not specifically claim washing of the precipitated protein in a saline solution (step h) or the specific centrifugation speed of 6000 rpm. Katopodis does not claim the extraction of lipid associated sialoprotein from CSF, urine, saliva, sputum, peritoneal fluid, pleural fluid and bronchial washings.

Chondros et al teach that the determination of total, lipid and bound sialic acid in body fluids other than serum has equally high sensitivity and specificity as the determination of total, lipid and bound sialic acid in serum(page 2105, column 1, lines 1-5 under the heading "Discussion"). Chondros et al teach the measurement of total, lipid and bound sialic acid in peritoneal fluid, pleural fluid and bronchial washings (Table I).

Stoscheck teaches that in many applications the solution containing the protein contains a mixture of components which can interfere with the measurement of protein, and that the interfering agent can be removed to facilitate the assay (page 57, last paragraph under "Colorimetric Assays"). Jones et al teaches a phosphate buffered saline wash after protein precipitation by trichloroacetic acid (column 21, lines 49-51).

It would have been prima facie obvious at the time the invention was made to substitute body fluids such as peritoneal fluid, pleural fluid and bronchial washings for the blood serum in the methods taught by Katopodis. One of skill in the art would have been motivated to do so by

the teachings of Chondros et al on the presence of protein bound sialic acids in said fluids and the teachings that fluids other than serum has equally high sensitivity and specificity as the determination of total, lipid and bound sialic acid. Regarding the specific limitation of claim 1, section (h) and claim 12 regarding the washing of the precipitate with saline, it is noted that optimization of the experimental protocol is within the purview of one of skill in the art, as exemplified by the teachings of Stoscheck regarding the removal of interfering components from protein before protein assays, and the example of Jones et al wherein proteins precipitated by trichloroacetic acid are washed by phosphate buffered saline.

Regarding the specific limitation of claim 1, sections (c) and claim 6 regarding the speed of centrifugation, it is noted that optimization of the experimental protocol is within the purview of one of skill in the art. Thus, it would have been prima facie obvious at the time the clamed invention was made that a centrifugation speed of 6000 rpm was obvious over the limitation of claim 9, in '346 specifying that centrifugation was carried out at about 3500 rpm for the extraction of lipid associated sialoprotein from bodily fluids.

8. All other rejections and objections as set forth or maintained in the Office action of Oct 22, 2002 are withdrawn.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A. Canella whose telephone number is (571)272-0828. The examiner can normally be reached on 11 am to 10 pm, except Wed, Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571)272-0832. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Karen A. Canella, Ph.D.
8/16/2005

Karen A. Canella
KAREN A. CANELLA PH.D
PRIMARY EXAMINER